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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/144,886	08/31/98	MARKS J	2307E-826US

020350 HM12/0310
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EXAMINER	
LEE, L	
ART UNIT	**PAPER NUMBER**
1645	11

DATE MAILED: 03/10/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/144,886	Marks et al
Examiner	**Group Art Unit**
Li Le	1645

☒ Responsive to communication(s) filed on Jan 4, 2000

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) 1-77 is/are pending in the applicat

Of the above, claim(s) 44-77 is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 1-43 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 9

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

— SEE OFFICE ACTION ON THE FOLLOWING PAGES —

DETAILED ACTION

Election/Restriction

1. Applicant's election with traverse of Group I, claims 1-43 in Paper No. 10 is acknowledged. The traversal is on the ground(s) that even though the claims are directed to distinct inventions, the examination of the entire application cannot constitute a serious burden , because the search for prior art relevant to Groups I-IV is essentially co-extensive. These arguments have been fully considered but not found to be persuasive for the reasons below.

In regard to burden of search and examination, MPEP 803 states that a burden can be shown if the examiner shows either separate classification, different field of search or separate status in the art. In the instant case a burden has been established in showing that the inventions of Groups I-IV are classified separately necessitating different searches of issued U.S. Patents. However, classification of subject matter is merely one indication of the burdensome nature of search. The literature search, particularly relevant in this art, is not co-extensive, because, for example, a search for an antibody binding to a specific epitope of the toxin will not cover the search for a method of neutralizing the toxin or a method of making an antibody. Additionally, it is submitted that the inventions of Groups I-IV have acquired a separate status in the art. Clearly different searches and issues are involved in the examination of each Group.

For reasons set forth in Office action mailed on 10/05/00 the restriction requirement is deemed to be proper and is therefore made FINAL.

Information Disclosure Statement

2. Items listed on form PTO-1449 have be considered by the examiner.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 6-10, 17-43 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 6-10, 17-43 are indefinite for using the term "variable heavy complementarity determining regions (CDRs) listed in Table 4" and "variable light complementarity determining regions (CDRs) listed in Table 4". There are different CDR regions in the antibodies VH region and VL region listed in Table 4 and these CDR regions are not clearly defined by specific sequence or by the specific property and characteristic. There are 47 different polypeptide sequences (SEQ ID NO:51-98) comprising these CDR regions listed in the Table 4, without clearly defined variable heavy/light complementarity determining regions (CDRs), one skilled in the art cannot determine when the metes and the bounds can be met.

Claims 17-21 are indefinite for using the term "framework region listed in Table 4". There are different framework regions in the antibodies VH region and VL region listed in Table

4 and these framework regions are not clearly defined by specific sequence or the property and characteristic. There are 47 different polypeptide sequences (SEQ ID NO:51-98) comprising these framework regions listed in the Table 4, without clearly defined variable heavy/light complementarity determining regions (CDRs), one skilled in the art cannot determine when the metes and the bounds can be met.

Claims 2-5, 11, and 30 are indefinite for using the term "the antibody of claim 1". It is not clear which antibody the applicant intent to indicate since there are two different antibodies in claim 1, an isolated antibody and an antibody expressed by a clone.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

6. Claims 1-11, 13-14, 17-30, 32-33, 36-43 are rejected under 35 U.S.C. 102(b) as being anticipated by Atassi et al (J Protein Chem 15 (7): 691-699, 1996 in Form 1449).

Atassi et al teach an isolated anti-botulinum neurotoxin type A (BoNT/A) antibody that specifically binds to an epitope of botulinum neurotoxin type A (BoNT/A) and the antibody can be used in a passive immunity/neutralizing against the toxin poisoning (Abstract and page 699).

The antibodies of Atassi et al were raised by the overlapping peptides of the entire Hc domain of BoNT/A (a highly protective domain of BoNT/A) which is the same antigen used to generate the claimed antibody in the instant application. Therefore, the antibodies of Atassi et al specifically bind to the epitopes specifically bound by an antibody expressed by a clone selected from clone, S25, C25, C39, 1C6, 1F3, or a clone listed Table 4. Because the antibodies of Atassi et al and the antibody expressed by the clones of the instant application are raised by the same protein containing same epitopes which have 4 amino acids in length identical to the epitopes in the BoNT/A Hc protein (specification, page 3, last paragraph to page 4).

7. Claims 1-43 are rejected under 35 U.S.C. 102(a) as being anticipated by Amersdorfer et al (Infect Immun 65 (9), 3743-3752, 1997).

Amersdorfer et al teach an isolated single-chain Fv (scFv) anti-botulinum neurotoxin type A (BoNT/A) antibody capable of neutralizing botulinum neurotoxin type A. The antibody of Amersdorfer et al specifically binds to an epitope of botulinum neurotoxin type A (BoNT/A) binding domain (Hc) (Abstract and Materials and Methods).

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. Claims 1-43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Atassi et al (J Protein Chem 15 (7): 691-699, 1996 in Form 1449) and Emanuel et al (J Immunol Meth 193: 189-197, 1996).

Atassi et al do not teach a single chain Fv (scFv) antibody or a (scFv)2 antibody that specifically binds to an epitope of Hc domain botulinum neurotoxin type A (BoNT/A). However, Emanuel et al teach a single chain antibody anti-BoNT/A generated by screening phage display libraries.

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to generate a single chain anti-BoNT/A antibody as taught by Emanuel et al using the antigen of Atassi et al because the known benefit of highly protective Hc domain of BoNT/A and due to the established advantages of recombinant phage display antibodies which include high specificity, reproducibility in assays, and provision for an unlimited supply of reagent. Thus, the claimed invention as a whole was clearly *prima facie* obvious.

Status of Claims

10. No claims are allowed. All claims stand rejected.

Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1645 by facsimile transmission. The faxing of such papers must conform with the notice

published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (703) 308-4242.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Li Lee whose telephone number is (703) 308-8891. The examiner can normally be reached on Monday-Friday from 8:30 AM to 5:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached at (703) 308-3995.

Li Lee
March 9, 2000

primary ALBERT NAVARRO
PATENT EXAMINER